

REGION SPECIFIC EFFECTS OF ANTIPSYCHOTIC DRUGS ON RAT  
STRIATAL NEUROTENSIN (NT) GENE EXPRESSION.

Kalpana M. Merchant, Dorcas J. Dobie, and Daniel M. Dorsa, Depts. of  
Psychiatry and Behavioral Sciences and Pharmacology, University of  
Washington, Seattle, WA 98195.

We have recently reported that acute administration of  
haloperidol dramatically increases expression of NT mRNA in the  
dorsolateral striatum (DLST) and shell region of the nucleus  
accumbens (sNA). The DLST effect appears to be due to an increase  
in transcription of the NT gene. We have compared these effects to  
those of other typical neuroleptics such as fluphenazine, and to the  
newer "atypical" agents which have a lower propensity to induce  
motor side effects such as clozapine, thioridazine, and remoxipride.  
In situ hybridization methods were used to quantify NT and c-Fos  
mRNA expression. While all antipsychotics increased sNA NT gene  
expression, only typical drugs affect NT gene transcription in DLST  
neurons. This difference was also noted when c-Fos mRNA  
expression was studied in the DLST of the same animals.  
Interestingly, the increase in sNA NT mRNA was not accompanied by  
a change in c-Fos message.

We have also studied the effects of chronic (4 week) treatment  
with haloperidol and with clozapine. We find that the DLST response  
to haloperidol is reduced over this time period, but not that of the  
sNA neurons. As with acute treatment, clozapine failed to alter  
DLST NT mRNA, but as with haloperidol it also caused a sustained  
elevation of sNA NT message expression. Taken together, these data  
suggest that the regional specificity of these responses may be  
related to the motor (DLST) and antipsychotic (sNA) effects of this  
class of drugs.